asserts that these "subsets" are new matter, and must be removed from the claims. The applicants respectfully traverse the rejection.

The original application, as filed, contained a full sequence of the human FEZ1 gene (SEQ ID NO: 1). Each of the claimed polynucleotides, which are portions of or homologous to SEQ ID NO: 1, contain the recited residues, were disclosed at least as part of SEQ ID NO: 1. The initially-disclosed sequences included all of the subsequences identified in the priority application. Therefore, the subject matter disclosed included both subsets for polynucleotides that are presently claimed and for those that are not presently claimed. Thus, applicants have disclosed a broad range of polynucleotides -- the polynucleotides claimed are not new matter.

The Examiner, at page 3 of the Advisory Action, states that "while the sequences are part of SEQ ID NO: 1, there is no support for any of the specific fragment and points recited. However, the fact that the specific endpoints are not individually recited is irrelevant. The applicants have disclosed the entire primary sequence of the strand. The applicants have disclosed that the invention is directed to portions of strands comprising, for example, at least twenty consecutive nucleotide residues. There is no functional criticality to the endpoints. The written description requirement under § 112 is satisfied when primary sequences of a claimed polynucleotide is provided, as is the case here. See, *e.g., Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 63 U.S.P.Q. 2d 1618 (Fed. Cir. 2002).

For at least the reasons above, it is requested that the Examiner reconsider and withdraw the rejection.

II. Rejection Under 35 U.S.C. § 112, First Paragraph: enablement.

At page 7-12 of the Office Action mailed March 11, 2002, the Examiner has rejected claims 118-121, 141, 142 and 144.

In the Advisory Action, the Examiner argues that the rejection under 35 U.S.C. § 112, first paragraph is a proper enablement rejection as the specification does not teach how to use the claimed pharmaceutical compositions. The Examiner also states, at page 3, that "regarding the claimed animal cells, applicants argue that the specification teaches enabled uses for them but does not point where these teachings can be found."

The Examiner's enablement rejection is based upon a flawed *Wands* analysis, with a particular focus on the alleged "complete lack of documented success for any gene therapy." The applicants again traverse the rejection.

The Examiner's analysis does not address any alleged absence of information in the specification that would allow a person of ordinary skill to make and use the invention, the correct test of enablement, but merely couches the operability rejection (*i.e.*, the idea that gene therapy does not work) in a *Wands* analysis.

Under the law, the Examiner carries the initial burden to establish a reasonable basis for questioning the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, (Fed. Cir. 1993); M.P.E.P. § 2164.04. The enablement requirement is satisfied if the specification describes any method for making and using the claimed invention that bears a "reasonable correlation" to the entire scope of the claims. 35 U.S.C. § 112, paragraph 1. In addition, although a patent application must provide an enabling disclosure at the time the application was filed, the application need not contain within its four corners all of the information necessary to practice the invention. M.P.E.P. § 2164.05(a). Information that was well known to persons of ordinary skill in the art need not be included in the application, and is preferably omitted. *In re Buchner*, 929 F.2d 660 (Fed. Cir. 1991). In this case, applicants respectfully submit that a person of ordinary skill, based upon the disclosure provided therein and given the sequences of peptides and/or nucleic acid molecules provided in the application, would find it well within the purview of routine skill to prepare pharmaceutical compositions and/or transfect animal cells in order to arrive at the claimed invention.

The Examiner concludes that the claims are non-enabled in consideration of four of the eight *Wands* factors. In forming the conclusion that any experimentation required is undue, one must weigh all of the *Wands* factors. M.P.E.P. 2164.01(a), citing *In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993). The *Wands* factors must be considered as a group in assessing compliance with the enablement requirement. *In re Wands*, 858 F2d 731 (Fed. Cir. 1988).

The Examiner states that the relevant claims are broad. As the Examiner admits, claims 118, 119, 120, 121, 141, and 142 all comprise a specific isolated polynucleotide. Such claims are not broad because they necessarily include a very narrow piece of subject matter, *i.e.*, a specific polynucleotide. The Examiner states next that "analysis of the prior art as of the effective filing date of the present application shows the complete lack of documented success for any treatment based on gene therapy," citing research papers regarding gene therapy that are characterized as unsuccessful. However, while unsuccessful research was available at the time of filing, so was successful research. See, for example, the following:

1. Cavazzana-Calvo M, Hacein-Bey S, de Saint Basile G, Gross F, Yvon E, Nusbaum P, Selz F, Hue C, Certain S, Casanova J-L, Bousso P, Le Deist F, Fischer A. Gene therapy of human severe combined immunodeficiency (SCID)-X1 disease. 2000 *Science* 288:669-672.

2. "Success of a hemophilia gene therapy experiment." January 1999 edition of the journal *Nature Medicine*

3. "Doctors announce gene therapy success for prostate cancer," Agence France Presse, Friday, October 22, 1999

> "Using gene therapy we re-educated the immune system to recognize prostate cancer cells as a potential infection and attack," said principal investigator in the study Jonathan Sions, an associate professor of oncology and urology at Johns Hopkins.

The Examiner concedes that the relative skill in the art is high. This high level of skill favors the applicants, as a greater quantity/complexity of experimentation is considered routine in high skill disciplines.

The Examiner states that the art of the invention is unpredictable. This is an incorrect application of *Wands*; the inquiry is not whether the general area of technology is predictable, but whether the techniques and information known and available in the art provide a reliable and reproducible basis for the practice of the invention, when coupled with the disclosure of the invention. M.P.E.P. 2164.04. In the present case the technology related to the production of polynucleotides pharmaceutical manufacturer, and the preparation of eukaryotic cells containing exogenous DNA was predictable.

Finally, applicants respectfully submit that the application provides a significant amount of direction along with working examples. Little experimentation would be required to make or use the invention based on the specification. Here, the Examiner has not met her burden of showing that any experimentation is undue, as her analysis fails to consider the evidence of enablement as a whole, as required under the law, but is rather based upon an apparent prejudice against so-called "gene therapy" inventions. Thus, the Examiner's *Wands* analysis provides no basis for a finding of non-enablement. It is requested that the Examiner reconsider and withdraw the § 112 first paragraph rejection for lack of enablement putting the claims in a position for allowance.

III. Drawing Corrections

The Examiner has stated that the proposed drawings are not acceptable because applicants have not submitted a marked up version of Figure 2b. Applicants point out that the revised drawing amendment format rules allow for corrections without submission of a marked up version. Applicants hereby incorporate by reference the previous comments and amendments related to Figure 2b, and respectfully request acceptance of Figure 2b under the new format rules.

CONCLUSION

In view of the foregoing, as well as the Amendment filed September 11, 2002, applicants submit that the claims are in a condition for allowance as they meet all the statutory requirements for patentability. Reconsideration and allowance of the claims at the Examiner's earliest opportunity is earnestly solicited.

Respectfully submitted,

CARLO M. CROCE, *et al.*

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(Date)

KRISTYNE A. BULLOCK
Registration No. 42,371
AKIN GUMP STRAUSS HAUER & FELD LLP
One Commerce Square
2005 Market Street, Suite 2200
Philadelphia, PA 19103-7013
Telephone: 215-965-1200
Direct Dial: 215-965-1348
Facsimile: 215-965-1210
E-Mail: kbullock@akingump.com

KAB:cmb
Enclosure
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